NOT FOR PUBLICATION

UNITED STATES DISTRICT COURT
DISTRICT OF NEW JERSEY

BRISTOL-MYERS SQUIBB CO., Plaintiff, v. APOTEX, INC., et al., Defendants.	CIVIL ACTION NO. 10-5810 (MLC) **MEMORANDUM OPINION & ORDER**

COOPER, District Judge

Plaintiff, Bristol-Myers Squibb Co. ("BMS"), commenced this action against defendants, Apotex, Inc. and Apotex, Corp. (collectively, "Apotex"), alleging, inter alia, that Apotex had filed an Abbreviated New Drug Application ("ANDA") with the United States Food and Drug Administration ("FDA") that would infringe four of its patents in violation of 35 U.S.C. § 271(e)(2). (See dkt. entry no. 1, Compl.)

The parties dispute the proper construction of claims throughout four of BMS's patents: United States Patent Nos. 6,596,746 ("the '746 Patent"), 7,125,875 ("the '875 Patent"), 7,153,856 ("the '856 Patent"), and 7,491,725 ("the '725 Patent"). The parties seek the Court's construction of these claims. The Court has considered the papers submitted by the parties, and heard oral argument on September 10, 2012, and October 2, 2012, and thereby conducted its Markman hearing. See

Markman v. Westview Instruments, Inc., 52 F.3d 967 (Fed.Cir. 1995), aff'd, 517 U.S. 370 (1996). Accordingly, the Court hereby issues the following findings of fact and conclusions of law with respect to its construction of the disputed claims of the '746 Patent, the '875 Patent, the '856 Patent, and the '867 Patent.

BACKGROUND AND FACTUAL FINDINGS

I. Background

A. ANDA Process

This action arises under the Drug Price Competition and Patent Term Restoration Act of 1984, Pub.L. No. 98-417, 98 Stat. 1585 (1984) (codified at 21 U.S.C. §§ 355, 360cc; 35 U.S.C. §§ 156, 271, 282), as amended by the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, Pub.L. No. 108-173, 117 Stat. 2066 (2003) (collectively, the "Hatch-Waxman Act").[1] Sale of a new drug is prohibited without approval from the FDA. 21 U.S.C. § 355(a). To obtain approval, a pioneering manufacturer must file a new drug application ("NDA") containing clinical studies of the drug's safety and efficacy. 21 U.S.C. § 355(b)(1). The manufacturer must also identify all patents that

[1] The Court is guided by the format used by the United States Court of Appeals for the Federal Circuit in citing the Hatch-Waxman Act. See, e.g., Janssen Pharmaceutica, N.V. v. Apotex, Inc., 540 F.3d 1353, 1355 (Fed.Cir. 2008).

claim the drug or a method of use. 21 U.S.C. § 355(b)(1)(G). The FDA publishes a list of drugs and the applicable patents in its Approved Drug Products With Therapeutic Equivalence Evaluations, known as the "Orange Book." Novo Nordisk A/S v. Caraco Pharm. Labs., Ltd., 601 F.3d 1359, 1361 (Fed.Cir. 2010).

A manufacturer seeking to market a generic copy of these listed drugs may submit an ANDA. 21 U.S.C. § 355(j). This abbreviated process streamlines FDA approval by allowing the generic manufacturer to rely on the safety and efficacy studies of a drug already listed in the Orange Book upon a showing of bioequivalence. 21 U.S.C. § 355(j)(2)(A)(iv). As part of the ANDA process, a generic manufacturer must certify one of four statements concerning the applicable listed drug: (I) no such patent information has been submitted to the FDA; (II) the patent has expired; (III) the patent is set to expire on a certain date; or (IV) the patent is invalid or will not be infringed by the manufacture, use, or sale of the generic drug ("Paragraph IV"). 21 U.S.C. § 355(j)(2)(A)(vii).

The Hatch-Waxman Act facilitates early resolution of disputes between pioneering and generic manufacturers by treating a Paragraph IV certification as an act of patent infringement. 35 U.S.C. § 271(e)(2). A generic manufacturer filing a Paragraph IV certification must provide the patentee

and the NDA holder with a detailed basis for its belief that the patent is invalid or not infringed. 21 U.S.C. § 355(j)(2)(B)(i). The patentee has forty-five days to sue the generic manufacturer for infringement. 21 U.S.C. § 355(j)(5)(B)(iii). If the patentee does not sue, then the FDA may approve the ANDA. If the patentee sues, then the FDA may not approve the ANDA until expiration of the patent, resolution of the suit, or thirty months after the patentee's receipt of notice, whichever is earlier. 21 U.S.C. § 355(j)(5)(B)(iii). "If the court determines that the patent is not invalid and that infringement would occur, and that therefore the ANDA applicant's paragraph IV certification is incorrect, the patent owner is entitled to an order that FDA approval of the ANDA containing the paragraph IV certification not be effective until the patent expires." Bayer AG v. Elan Pharm. Research Corp., 212 F.3d 1241, 1245 (Fed.Cir. 2000) (internal citation omitted).

B. The Parties

BMS is a Delaware corporation with its principal place of business in New York and multiple research and development sites in New Jersey. (See Compl. at ¶ 2.) BMS is the assignee of the '746 Patent, the '875 Patent, the '856 Patent, and the '725 Patent. (See id. at ¶¶ 16-23.)

BMS markets the drug dasatinib under the trade name of Sprycel© for the treatment of cancer, including chronic myeloid leukemia ("CML"); the drug and methods of use are covered by the suite of four patents. (See dkt. entry no. 62, Pl. Opening Claim Construction Br. at 1 ("Pl. Opening Br.").) The '746 Patent claims, inter alia, the compound dasatinib. (See id.) The '875 Patent claims methods of using dasatinib to treat cancer, including treatment of CML. (See id.) The '856 Patent claims methods of using dasatinib to treat cancer via oral administration. (See id.) The '725 Patent claims, inter alia, a crystalline monohydrate form of dasatinib. (See id.) BMS holds a NDA approved by the FDA for dasatinib tablets, NDA No. 21-986. (See Compl. at 24.)

Apotex, Inc. is incorporated in Canada, and Apotex Corp. is a Delaware corporation with a place of business in Florida. (See Compl. at ¶¶ 3-4.) Apotex Corp. serves as the marketing and sales affiliate in the United States for Apotex, Inc. (See id. at ¶ 5.) Pursuant to Section 505 of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 355(a), Apotex filed an ANDA for dasatinib tablets with the FDA. (See id. at ¶ 26.) Apotex wishes to manufacture, use, import, and sell a generic dasatinib tablet, which would have the same indications as BMS's Sprycel© product. (See id. at ¶¶ 26-31.) BMS alleges that Apotex's

generic dasatinib tablet infringes the '746 Patent, the '875 Patent, the '856 Patent, and the '725 Patent. (See id. at ¶ 31.) Apotex sent written notice to BMS of its ANDA filing declaring, inter alia, noninfringement and invalidity as to the '746 Patent, the '875 Patent, the '856 Patent, and the '725 Patent. (See id. at ¶ 28.) BMS asserts claims 6, 7, 18, 27-30, 32, 33, 42-44, and 46-48 of the '746 Patent; claims 1-3, 5, 7, 9-12, 14, and 27 of the '875 Patent; and claim 1 of the '856 Patent. (See Pl. Opening Br. at 1.) From the '725 Patent, BMS asserts claims 1-16. (See id. at 2.)

The asserted claims overlap in some combinations of the various terms in dispute. For instance, claim 6 of the '746 Patent contains the terms "salt", "compound", "selected from a group consisting of" and a chemical name, whereas claim 43 of the '746 Patent employs the terms "salt", "compound" and a chemical structure. (See '746 Patent at col. 276, lines 51-53; col. 302, lines 9-19.) Where advisable, the Court has addressed the terms together, but similar to how the parties addressed the terms in the papers, some terms were also construed individually. (See, e.g., Pl. Opening Br. at 5-7; dkt. entry no. 63, Defs. Opening Claim Construction Br. at 5-8 ("Defs. Opening Br.").)

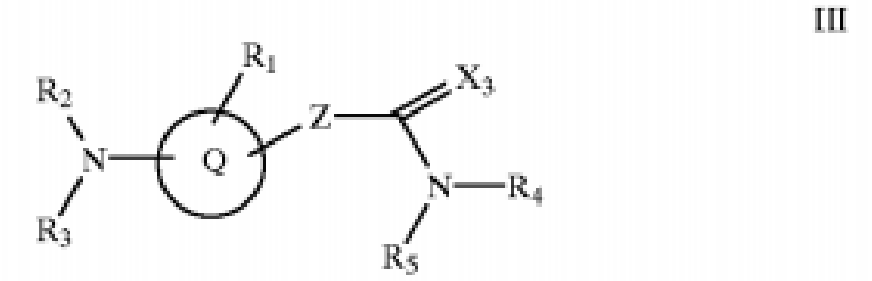
II. The Patents

A. The '746 Patent

The '746 Patent discloses "[n]ovel cyclic compounds and salts thereof, pharmaceutical compositions containing such compounds, and methods of using such compounds in the treatment of protein tyrosine kinase-associated disorders such as immunologic and oncologic disorders." ('746 Patent, Abstract.) One of the compounds covered by the patents at issue is dasatinib; the drug works as a treatment for CML, which is tied to the "Philadelphia Chromosome." (See dkt. entry no. 86, Tr. of Markman Hr'g on Sept. 10, 2012 at 7 ("9-10-12 Transcript").) The Philadelphia Chromosome is a mutated gene, created as a result of a fusion of chromosome 9 and chromosome 22. (See id.) This gene causes an overproduction of tyrosine kinase, an enzyme. (See id.) Tyrosine kinase is a key element in the regulation of cell signaling, including cell proliferation and cell differentiation. ('746 Patent at col. 1, lines 19-21.) Enhanced activity of the enzyme causes the proliferation of malignant and nonmalignant cells, which can lead to CML. (See id. at col. 1, lines 35-44; see also 9-10-12 Transcript at 7.) Dasatinib is an inhibitor of tyrosine kinase. (See 9-10-12 Transcript at 7.)

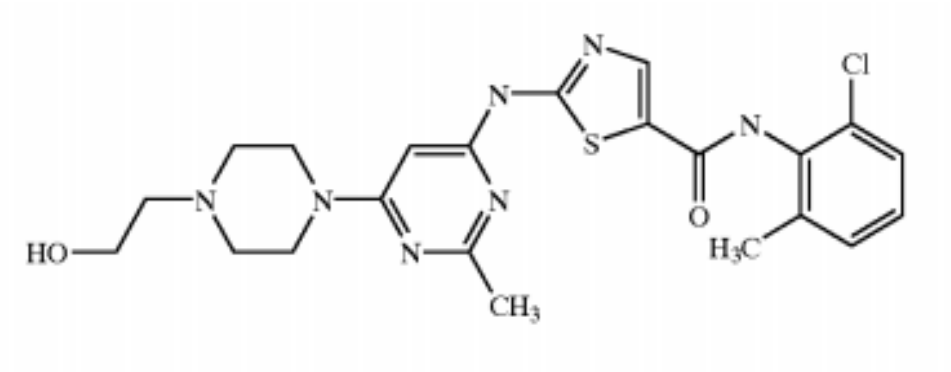
The '746 Patent is composed of 49 claims, of which claims 1, 3, 4, 6, 7, and 43 are independent. ('746 Patent at cols. 269–302.) Phrases found in claims 6, 7, 43, 44, and 47 of the '746 Patent require construction. Claim 6 describes "[a] compound or salt thereof selected from the group consisting of . . . 'N-(2-Chloro-6-methylphenyl)-2-[[6-[4-(2-hydroxyethyl)-1-piperazinyl]-2-methyl-4-pyrimidinyl]amino-5-thiazolecarboxamide."[2] (Id. at col. 276, lines 51-53 and col. 292, lines 46-48.) Claims 7, 44, and 47 all contain similar language requiring construction by the Court, as exemplified by the specific phrases in Claim 7:

> A method for the treatment of a protein tyrosine kinase-associated disorder, comprising the step of administering to a subject in need thereof an amount effective therefor of at least one compound of formula III or a salt thereof:



[2] Claim 6 includes several pages of different chemical names, but the parties have both focused on this particularly identified chemical. (See, e.g., Pl. Opening Br. at 7-8; see also Defs. Opening Br. at 7-11.)

(Id. at col. 297, lines 38-50 (emphasis added); see id. at col. 302, lines 20-22, 28-31.) Claim 43 requires construction as well: "The compound



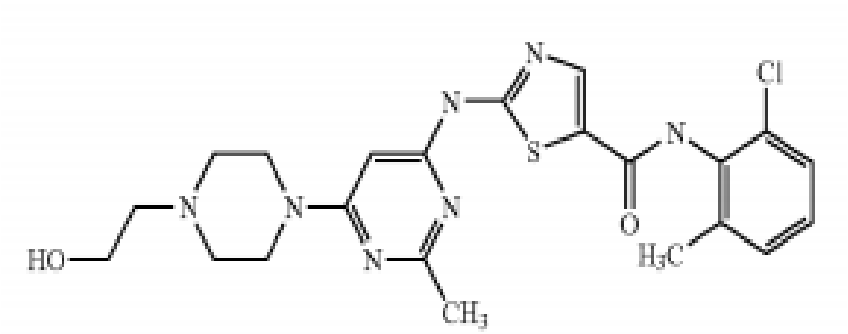
including salts thereof." (Id. at col. 302, lines 9-19.)

B. The '856 Patent

BMS is the assignee of the '856 Patent, which discloses "[n]ovel cyclic compounds and salts thereof, pharmaceutical compositions containing such compounds, and methods of using such compounds in the treatment of protein tyrosine kinase-associated disorders such as immunologic and oncologic disorders." ('856 Patent, Abstract.) The '856 Patent issued from a continuation application of the '746 Patent. (See Pl. Opening Br. at 1.) The patent claims methods of using dasatinib to treat cancer via oral administration. (See id.)

The parties request construction of phrases in the asserted claim 1: "A method for treatment of cancer, comprising

the step of administering orally to a subject in need thereof an amount effective therefor of the compound



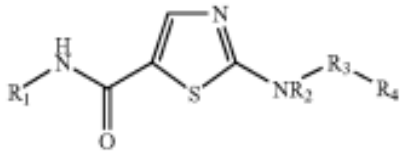
or salts thereof." ('856 Patent at col. 278, lines 53-67 (emphasis added); see Pl. Opening Br. at 9-15; see also Defs. Opening Br. at 8-14.)

C. The '875 Patent

BMS is the assignee of the '875 Patent, which was filed on March 24, 2003, and issued on October 24, 2006. The '875 Patent discloses "[n]ovel cyclic compounds and salts thereof, pharmaceutical compositions containing such compounds, and methods of using such compounds in the treatment of protein tyrosine kinase-associated disorders such as immunologic and oncologic disorders." ('875 Patent, Abstract.)

The parties seek construction of phrases that are repeated in claims 1, 2, 3, 11, and 27. The language in claim 1 serves as an example: "A method for the treatment of a cancer comprising administering to a subject in need thereof an

effective amount of the compound of formula III or a salt thereof:

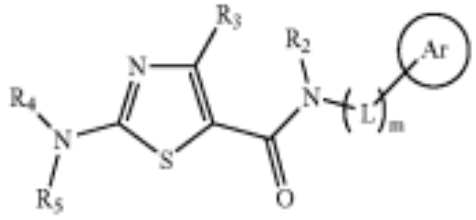


." (Id. at col. 276, lines 51-63 (emphasis added).) The phrase "administering to" appears in claims 1, 2, 3, 11, and 27. (See id. at col. 276, line 54; id. at col. 277, lines 11, 35; id. at col. 278, line 42.) The phrase "administered . . . to" appears in claim 5. (See id. at col. 277, line 66.)

A phrase that is repeated in claims 9, 10, and 27, and a similar phrase in 12 and 16, require construction. Claim 9 provides one example: "The method of claim 1 wherein the cancer is resistant to treatment by STI-571." (Id. at col. 278, lines 36-37 (emphasis added); see id. at col. 278, lines 38-39.) Claim 12 provides the other: "The method of claim 11, wherein the chronic myelogenous leukemia (CML) is resistant to STI-571." (Id. at col. 278, lines 60-61 (emphasis added).)

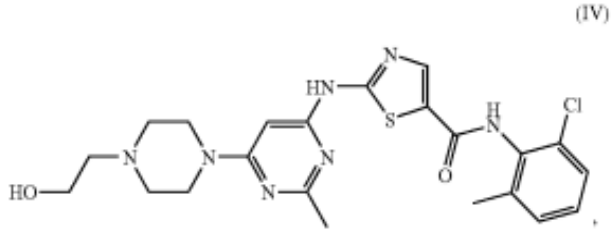
D. The '725 Patent

BMS is the assignee of the '725 Patent, which was filed on July 29, 2005, and issued on February 17, 2009. The '725 Patent discloses "processes for preparing compounds having the formula



and crystalline forms thereof, wherein Ar is aryl or heteroaryl, L is an optional alkylene linker, and R_2, R_3, R_4, and R_5, are defined as in the specification herein, which compounds are useful as kinase inhibitors, in particular, inhibitors of protein tyrosine kinase and p38 kinase." ('725 Patent, Abstract.) The patent claims, inter alia, a crystalline monohydrate form of dasatinib, and it is not tied closely with the other three patents at issue in this suit. (See Pl. Opening Br. at 1.) The patented invention represents an improvement in making 2-aminothiazole-5-carboxamides over previously disclosed processes. (See '725 Patent at col. 3, lines 1-10.) The prior art disclosed methods that had "drawbacks with respect to the production of side products, the use of expensive coupling reagents, less than desirable yields, and the need for multiple reaction steps to achieve the 2-aminothiazole-5-carboxamide compounds." (Id. at col. 3, lines 6-10.)

From claims 1, 3, and 12, the parties request construction of the phrase "crystalline monohydrate of the compound of formula (IV)



." (Id. at col. 48, lines 48-61.) The parties also request construction of the phrase "which is characterized by an x-ray powder diffraction pattern substantially in accordance with that shown in FIG. 1," found in claim 1. (Id. at col. 48, lines 62-63.) Claim 2 requires construction of the first part of the claim: "The compound of claim 1"; the Court will construe the rest of the claim separately: "which is characterized by differential scanning calorimetry thermogram and a thermogravimetric analysis substantially in accordance with that shown in FIG. 2." (Id. at col. 48, lines 64-66.)

The parties request construction for the similar phrases of "[t]he compound of claim 1," "[t]he compound of claim 3," "[a] process for preparing the compound of claim 3," "[t]he compound of claim 9," and "[t]he compound of claim 12." (See Pl. Opening Br. at 21; see also Defs. Opening Br. at 34-36.) These phrases come from claims 2, 4-11, and 13-16. (See '725 Patent at col.

48, line 64; see also id. at col. 49, lines 20, 22, 32, 36, 39; id. at col. 50, lines 1, 6, 9, 30, 33, 35, 37.)

From claim 3, the following phrase needs construction: "which is characterized by an x-ray powder diffraction pattern (CuK$_\alpha$ λ=1.5418 Å at a temperature of about 23°C.) comprising four or more 2θ values selected from the group consisting of 18.0±0.2, 18.4±0.2, 19.2±0.2, 19.6±0.2, 21.2±0.2, 24.5±0.2, 25.9±0.2, and 28.0±0.2."[3] (Id. at col. 49, lines 14-18.) From Claim 5, the parties seek construction of

> characterized by unit cell parameters approximately equal to the following dimensions: Cell dimensions: a(Å)=13.8632(7); b(Å)=9.3307(3); c(Å)=38.390(2); Volume=4965.9(4) Å^3
> Space group Pbca
> Molecules/unit cell 8
> Density (calculated) (g/cm^3) 1.354.

(Id. at col. 49, lines 23-32.) Additionally, the parties request construction of a phrase from claims 8, 15, and 16: "wherein the compound is substantially pure." (Id. at col. 49, lines 39-40; id. at col. 50, lines 35-38.) From claim 9, two phrases require construction: "being further characterized by a differential scanning calorimetry having a broad peak between

[3] A certificate of correction was filed on May 11, 2010 to correct the typographical error that resulted in a gamma symbol instead of lambda. (See dkt. entry no. 62-1, Decl. of Jerry Atwood, Ex. M.) Accordingly, the text will be construed by the Court as if it read "CuK$_\alpha$ λ=1.5418 Å" instead of "CuK$_\alpha$ γ=1.5418 Å."

approximately 95° C. and 130° C." and "which corresponds to the loss of one water of hydration on thermogravimetric analysis". (Id. at col. 50, lines 2-5.)[4] These two phrases are repeated in claim 12. (Id. at col. 50, lines 25-28.)

In claim 10, the phrase "which is further characterized by a weight loss of 3.48% by thermogravimetric analysis between 50° C. and 175° C." also requires construction. (Id. at col. 50, lines 6-8.) In claim 11, the phrase "wherein the differential scanning calorimetry further has a peak at approximately 287°C." requires construction. (Id. at col. 50, lines 9-11.)

DISCUSSION AND CONCLUSIONS OF LAW

I. Applicable Legal Standards

The Court must determine the scope and meaning of the patent claims as a matter of law. Markman, 52 F.3d at 979. Claim terms "are generally given their ordinary and customary meaning." Phillips v. AWH Corp., 415 F.3d 1303, 1312 (Fed.Cir. 2005) (quotation omitted). The ordinary and customary meaning of a claim term is the meaning a "person of ordinary skill in the art in question" would give to such term on the effective

[4] The typographical error of inserting "13° C." instead of "130° C." and misspelling "thermogravimetric" as "thermogravitmetric" has also been corrected through the same certificate of correction. (See Decl. of Jerry Atwood, Ex. M.) Accordingly, the Court will read the term as "thermogravimetric" and the temperatures as "95°C. and 130°C."

filing date of the patent application. Id. at 1313. Such a person is deemed to interpret the claim term in the context of the entire patent, including the specification and prosecution history. See id. It is appropriate to deviate from the "ordinary" meaning of a claim term when the intrinsic evidence, including the specification and prosecution history, "reveal[s] a special definition given to a claim term by the patentee that differs from the meaning it would otherwise possess." Id. at 1316.

The specification is "always highly relevant to the claim construction analysis" and is "the single best guide to the meaning of a disputed term." Honeywell Int'l, Inc. v. ITT Indus., Inc., 452 F.3d 1312, 1318 (Fed.Cir. 2006) (internal quotation omitted). The specification may contain an intentional disclaimer or a disavowal of claim scope by the inventor, in which case the inventor's intention, as expressed in the specification, is dispositive. Phillips, 415 F.3d at 1316. It is, however, improper to read a limitation from the specification into the claims. See Teleflex, Inc. v. Ficosa N. Am. Corp., 299 F.3d 1313, 1326 (Fed.Cir. 2002).

The Court also considers the patent's prosecution history. Phillips, 415 F.3d at 1317. The prosecution history provides evidence of how the inventor understood the patent. See id.

The prosecution history also demonstrates whether the inventor limited the invention during the course of the patent prosecution, thus narrowing the scope of the ultimately patented product. See id. The prosecution history reflects the ongoing negotiations between the inventor and the United States Patent and Trademark Office ("PTO"), and thus is often less clear and less useful than the specification. See id.

The Court may in certain circumstances consider "extrinsic evidence," including "expert and inventor testimony, dictionaries, and learned treatises." Id. In general, such evidence is less reliable than its intrinsic counterparts. See id. at 1318. In some situations, the ordinary meaning of claim language as understood by a person of skill in the art will be readily apparent, and claim construction will then involve the simple application of the widely accepted meanings of commonly understood words. See id. at 1314. In such circumstances, general purpose dictionaries may be helpful. See id. Nonetheless, "heavy reliance on the dictionary divorced from the intrinsic evidence risks transforming the meaning of the claim term to the artisan into the meaning of the term in the abstract, out of its particular context, which is the specification." Id. at 1321. Also, expert evidence may be useful for certain limited purposes, but unsupported assertions

by experts as to the definition of a claim term are not useful, and the after-the-fact testimony of the inventor is accorded little, if any, weight in the claim construction inquiry. See id.

If, after applying these principles, the Court concludes that a claim term remains "insolubly ambiguous," it must hold that the claim limitation is indefinite. Honeywell Int'l, Inc. v. Int'l Trade Comm'n, 341 F.3d 1332, 1340-42 (Fed.Cir. 2003). When that occurs, the Court must strike down all claims of which the term is a part as indefinite and therefore invalid pursuant to 35 U.S.C. § 112. See id. at 1338-39; see also Aero Prods. Int'l, Inc. v. Intex Recreation Corp., 466 F.3d 1000, 1015-16 (Fed.Cir. 2006).

II. Legal Standards Applied Here

A. Construction of the '746, '875, and '856 Patents

1. "A compound or salt thereof selected from the group consisting of"

Claim 6 specifies a "compound or salt thereof selected from the group consisting of," and it is directed to a compound or salt selected from a list of compounds that includes dasatinib. ('746 Patent at col. 6, lines 18-35.)

BMS proposes that the disputed term be given its plain meaning as understood by a person of ordinary skill in the art:

"a compound or its salt selected from the claimed list." (Pl. Opening Br. at 5-7.) BMS argues that "selected from the group consisting of" constitutes a form of alternative expression commonly known as a Markush group, which limits the claimed "compound or salt thereof" to those compounds which are specifically named in claim 6. (Id. at 5 (citing Manual of Patent Examining Procedure § 2173.05(h) (8th ed. 2001)).) BMS argues that Apotex incorrectly assumes that the Markush group concerns the purity of the claimed invention, when the patent instead discloses that claimed compositions may contain other ingredients besides the listed compounds for other preservation, delivery, or dilution purposes. (See id. at 6-7.) BMS would further read "salt" as it is defined in the '746 Patent specification: "acidic and/or basic salts formed with inorganic and/or organic acid or bases." (Id. at 6.)

Apotex argues that the term "compound" should be construed "to reflect the specification's express lexicography statements, so the term includes prodrugs, solvates, salts and stereoisomers of any particularly listed compound or structure." (Defs. Opening Br. at 5.) Accordingly, Apotex would have all salts included in the term "compound" as well: "the term 'compound' should conform to the specification's clear statement that the term encompasses 'salts'; 'prodrugs and solvates of the

compound[]'; and 'stereoisomers of the ... compound[]' or salt thereof." (Id. at 5-6.) Apotex would draw the definition for "salt" from language included in the specification:

> The term "salt(s)", as employed herein, denotes acidic and/or basic salts formed with inorganic and/or organic acids and bases. Zwitterions (internal or inner salts) are included within the term "salt(s)" as used herein (and may be formed, for example, where the R substituents comprise an acid moiety such as a carboxyl group). Also included herein are quaternary ammonium salts such as alkylammonium salts. Pharmaceutically acceptable (i.e., non-toxic, physiologically acceptable) salts are preferred, although other salts are useful, for example, in isolation or purification steps which may be employed during preparation.

(Id. at 6 (quoting '746 patent at col. 6, lines 21-31).) Finally, relying on the claim construction reasoning of Abbott Labs. v. Baxter Pharm. Prods., Inc., 334 F.3d 1274, 1280-81 (Fed.Cir. 2003), Apotex contends that the Markush group language "precludes mixtures of the listed compounds and other compounds not part of the list, including impurities." (Defs. Opening Br. at 7.)

The court in Abbott Labs. reasoned that a patentee's use of "a" in conjunction with a Markush grouping should be construed to exclude mixtures, including a mixture of compounds within the Markush group list itself. Abbott Labs., 334 F.3d at 1281 ("'a' with 'consisting of' in this case indicates only one member of a Markush group. . . . If a patentee desires mixtures or

combinations of the members of the Markush group, the patentee would need to add qualifying language while drafting the claim" such as "and mixtures thereof" or "at least one member of the group"). Apotex submits that, based on this, the patentee's failure to include any qualifying language in the '746 Patent requires the Court to construe the claim so that "[a]ny substance that mixes two compounds on the list (whether or not as an impurity), or mixes one compound on the list and one off the list, is outside the scope of this claim language." (Defs. Opening Br. at 8.)

BMS replies that the disjointed treatment Apotex gives the language in claim 6 introduces unnecessary ambiguity to avoid applying the plain meaning of the terms. (See dkt. entry no. 66, Pl. Responsive Claim Construction Br. at 4 ("Pl. Responsive Br.").) BMS further argues that the claim language at issue in Abbott Labs. was directed at a "composition" in combination with Markush group terms. (See id. at 5.) BMS argues that the case cited by Apotex is distinguishable from the present claim language because Abbott Labs. does not address whether use of the phrase "consisting of" without "a" precludes impurities in a preparation of the compound. See Abbott Labs., 334 F.3d at 1276, 1281; see also Teva Pharm. USA Inc. v. Amgen, Inc., No. 09-5675, 2010 U.S. Dist. LEXIS 95288, at *20-21 (E.D.Pa. Sept.

10, 2010) (rejecting proposed construction that use of a Markush group means that "there can be only one member of the Markush group present in a product and, if there are more, then the product is outside the scope of the patent"). (See Pl. Responsive Br. at 4-5.)

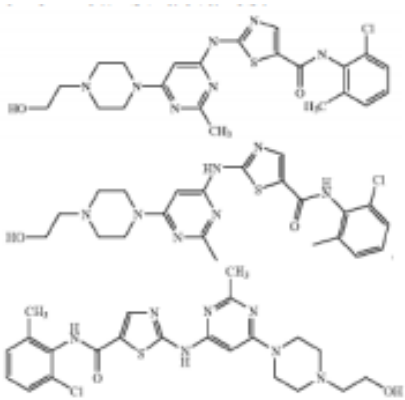
The Court has considered the patent claims and specification, as well as the parties' respective arguments. The Court agrees with the patentee that the Markush group language is here properly utilized to include any pharmaceutical composition containing a compound listed in the claim. The definitions for "compound" and "salt" proposed by Apotex rely on phrases pulled out of context from the specification that are not properly applied to the claims in order to distort its construction. The Court construes the term "a compound or salt thereof selected from the group consisting of" to conform with the patentee's requested definition, namely the plain meaning of the term as understood by a person of ordinary skill in the art:

"[A] compound or its salt ('salt' meaning acidic and/or basic salts formed with inorganic and/or organic acid and bases) selected from the claimed list."

2. Chemical names identified in Claim 6 including "'N-(2-Chloro-6-methylphenyl)-2-[[6-[4-(2-hydroxyethyl)-1-piperazinyl]-2-methyl-4-pyrimidinyl]amino-5-thiazolecarboxamide"

Claim 6 lists many chemical names, including a "'N-(2-Chloro-6-methylphenyl)-2-[[6-[4-(2-hydroxyethyl)-1-piperazinyl]-2-methyl-4-pyrimidinyl]amino-5-thiazolecarboxamide." ('746 Patent at col. 292, lines 46-48.) The chemical names form a list of compounds that includes dasatinib. ('746 Patent at col. 6, lines 18-35.)

The patentee has proposed a construction of the term as follows: "'N-(2-Chloro-6-methylphenyl)-2-[[6-[4-(2-hydroxyethyl)-1-piperazinyl]-2-methyl-4-pyrimidinyl]amino-5-thiazolecarboxamide represents the compound having the following equivalent chemical structures:



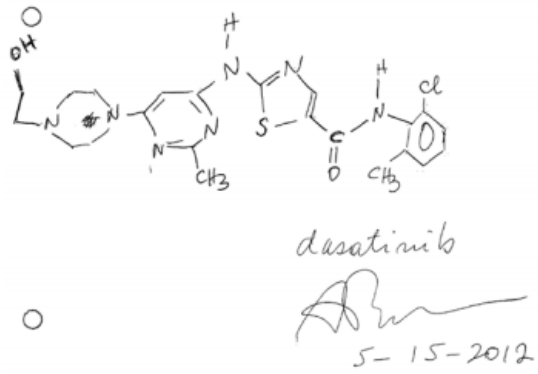
." (See dkt. entry no. 51, Joint Claim Construction & Prehearing Statement, Ex. 2 at 2 ("Joint Statement").) BMS offers the opinion of an expert to confirm

that a person of ordinary skill in the art would interpret the claim consistently with this plain reading and would further recognize that the recited name is that of dasatinib. (See Pl. Responsive Br. at 6.)

Apotex counters that "[t]he chemical descriptors given in claim 6 require the plain and ordinary meaning of such terms, to be interpreted according to [International Union of Pure and Applied Chemistry ("IUPAC")] nomenclature guidelines." (Joint Statement at 2.) In support of its position, Apotex relies on an expert, who claims that the IUPAC standard is the globally recognized chemical nomenclature guide and that the name should be construed under the IUPAC rules. (See Defs. Opening Br. at 9.) Apotex argues that 'N-(2-Chloro-6-methylphenyl)-2-[[6-[4-(2-hydroxyethyl)-1-piperazinyl]-2-methyl-4-pyrimidinyl]amino-5-thiazolecarboxamide, when properly read under IUPAC's naming conventions, is not equivalent to dasatinib. (See id.) Apotex specifically argues that, because two hydrogen atoms that would be bound to two nitrogen atoms are not included on the chemical structure pictured in Example 455 of the '746 Patent, dasatinib is not an equivalent structure. (See id. at 10.) Apotex also seeks to have the Court construe "'N-(2-Chloro-6-methylphenyl)-2-[[6-[4-(2-hydroxyethyl)-1-piperazinyl]-2-methyl-4-pyrimidinyl]amino-5-thiazolecarboxamide" in such a way as to

exclude the chemical dasatinib. (See id. at 10-11.) Apotex's expert provides that dasatinib is not included in the three equivalent chemical structures that BMS would have the Court construe as the meaning of this term. (See id. at 9-10.)

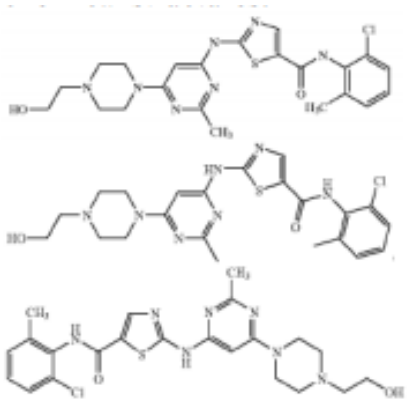
BMS responded both in the papers and at oral argument that it is a common understanding in the relevant art that chemical illustrations representing real chemical structures employ some shorthand, i.e., not every hydrogen atom in the chemical compound must be depicted. (See Pl. Opening Br. at 8; see also 9-10-12 Transcript at 77-78.) BMS also points out that, when Apotex's expert was asked to draw out the structure associated with 'N-(2-Chloro-6-methylphenyl)-2-[[6-[4-(2-hydroxyethyl)-1-piperazinyl]-2-methyl-4-pyrimidinyl]amino-5-thiazolecarboxamide, he drew the following depiction, and then identified the chemical structure as that of dasatinib:



. (See Pl. Responsive Br. at 6-7.)

The Court has considered the parties' respective arguments, the patent claims and specification, and the extrinsic evidence of expert opinions proffered by the parties. The Court agrees with the patentee that chemical structures sometimes are depicted without every hydrogen atom drawn onto the structure; such failure to show the hydrogen atoms on the chemical structures depicted in the patent will not preclude the Court from construing the term to include an equivalent structure with the hydrogen atoms present. Further, the Court rejects Apotex's proposal to exclude dasatinib from the scope of the named term 'N-(2-Chloro-6-methylphenyl)-2-[[6-[4-(2-hydroxyethyl)-1-piperazinyl]-2-methyl-4-pyrimidinyl]amino-5-thiazolecarboxamide because its own expert recognized that, when drawn, the term represents a structure equivalent to and recognizable to a person of ordinary skill in the art as being dasatinib. The Court thus construes the term "'N-(2-Chloro-6-methylphenyl)-2-[[6-[4-(2-hydroxyethyl)-1-piperazinyl]-2-methyl-4-pyrimidinyl]amino-5-thiazolecarboxamide" as follows:

the compound having the following equivalent chemical structures



.

3. "A method for the treatment of a protein tyrosine kinase-associated disorder, comprising the step of administering to a subject in need thereof an amount effective therefor of at least one compound of formula III or a salt thereof"

The terms "administering to" or "administering orally to" and "subject in need thereof" appear in claims 7, 44, and 47 of the '746 Patent, claim 1 of the '856 Patent, and claims 1, 2, 3, 11, and 27 of the '875 Patent. These claims are directed to treating a protein tyrosine kinase-associated disorder with at least one compound of formula III or a salt thereof.

a. "Administering to" or "administering orally to"

BMS proposes that the term be construed with the help of an extrinsic source, the Merriam-Webster's Collegiate® Dictionary, to mean "to mete out or dispense or to give remedially [the compound in oral form, including but not limited to tablets, capsules, granules or powders]." (Pl. Opening Br. at 9.) BMS

argues that, because the term was not explicitly defined in the patent at issue, extrinsic evidence is available to "aid the Court's understanding of the patent." See Wright Med. Tech., Inc. v. Osteonics Corp., 122 F.3d 1440, 1443 (Fed.Cir. 1997). (See Pl. Opening Br. at 9.)

BMS further argues that dictionaries are acceptable aids as extrinsic evidence and that a similar dictionary definition of "administering" has previously been accepted by courts construing similar claim language. See Phillips, 415 F.3d at 1318; see also Acorda Therapeutics, Inc. v. Apotex, Inc., No. 07-4937, 2011 WL 4074116, at *3, 26 (D.N.J. Sept. 6, 2011), aff'd, 476 Fed.Appx. 746 (Fed.Cir. 2012) (construing a term in a patent concerning a method of administering tizanidine multiparticulates to patients with food as meaning "giving, dosing, self-dosing or taking of the composition" with specific plasma concentration results). (See Pl. Opening Br. at 9.) BMS also argues that when the patent (which specifies various routes of administration) is read as a whole, the term "administering to" can be seen as distinct from any particularly specified route of administration. (See id. at 10.)

Apotex proposes a construction with two components: (1) "administering" refers to an administration alone or in combination, in a single dose or in divided doses, with or

without other agents, simultaneously or in succession; and (2) two actors are required: the subject in need thereof and the person responsible for giving the therapeutic agent. (See Defs. Opening Br. at 15; see also Joint Statement at 3.) Apotex relies on prosecution history and expert testimony in addition to legal argument to bolster this construction. (See Joint Statement at 3.)

Apotex argues that this construction of "administering" reflects the expansive teachings in the specification without "introducing extraneous or other limiting elements into the claim term." (Defs. Opening Br. at 15.) Because the specification teaches that such methods of "administering" can occur, Apotex argues that the definition can and should include those methods without placing limitations on the meaning beyond the teachings of the patent. (See id.) Apotex argues that the significance of "to" is made clear by examining the "claim language and . . . syntactic signs of its meaning." (Id. (citing Eastman Kodak Co. v. Goodyear Tire & Rubber Co., 114 F.3d 1547, 1553 (Fed.Cir. 1997), abrogated on other grounds by Cybor Corp. v. FAS Techs., Inc., 138 F.3d 1448 (Fed.Cir. 1998)).) The term "administering to" or "administering orally to" requires two actors: one who gives the agent and a subject who is in need of treatment. (See id. at 16.) Apotex argues

that where a patentee has drafted a claim term implying there is more than one actor, the patentee cannot then ask the Court to penalize a single actor defendant who does not perform or fulfill the claim in its entirety. (See id. at 16-17.)

BMS responds that case law does not support Apotex's position: Eastman Kodak encourages courts to look to syntactic context for signals of the meaning of "to". See Eastman Kodak, 114 F.3d at 1553. (See Pl. Responsive Br. at 9.) Here, the only verb providing any such signal is "administering" and a single actor is required for that. (See id. at 9-10.) "To" is merely used to suggest a direction - toward the subject in need thereof, who is not required to take any action to fulfill the claim. (See id. at 10.) BMS also relies on Acorda Therapeutics, Inc. for the proposition that such a term in a claim could be fulfilled by a physician, pharmacist, or patient alone. See Acorda Therapeutics, Inc., 2011 WL 4074116 at *27. Finally BMS argues that two actors are not required for infringement even though animals are included in the potential treatment population, thus identifying a population needing the drug but unable to self-administer. (See Pl. Responsive Br. at 10.) BMS argues that this demonstrates the only actor targeted by the claim is the one performing the administration of the drug. (See id.) Apotex's responsive brief argues that the

term, when read in context, requires two actors. (See dkt. entry no. 69, Defs. Responsive Claim Construction Br. at 13-14 ("Defs. Responsive Br.").)

The Court has considered the parties' respective arguments, the patent claims and specification, and the extrinsic evidence proffered by the parties. The Court agrees with the patentee that the term neither requires multiple actors nor specifies any particular route of administration. The Court thus construes the terms "administering to" or "administering orally to" as follows:

To mete out or dispense or to give remedially.

b. "a subject in need thereof"

BMS argues that this term should be given its plain meaning as understood by a person of ordinary skill in the art. (See Pl. Opening Br. at 11.) BMS proposes that the term be construed to mean "an animal, including a human, in need thereof". (Joint Statement at 4.) For support, BMS relies on the specification, which states "preferred subjects for treatment include animals, most preferably mammalian species such as humans, and domestic animals such as dogs, cats, and the like . . . ." ('746 Patent at col. 26, lines 53-57.) Quoting Phillips, BMS further argues that the specification should serve as the "primary basis for

construing the claim" and as the "best source for understanding a technical term." See Phillips, 415 F.3d at 1315. Finally, BMS argues that Apotex's construction would impermissibly broaden the meaning by extending its reach to "any living organism", which is in direct contravention of the more limited sphere envisioned by the specification. See ERBE Elektromedizin GmbH v. Int'l Trade Comm'n, 566 F.3d 1028, 1034 (Fed.Cir. 2009) ("We generally do not construe claim language to be inconsistent with the clear language of the specification. Usually [the language of the specification] is dispositive.") (internal citation omitted). (See Pl. Opening Br. at 11.)

Apotex proposes that the term be construed to mean: "Any living organism having a protein-kinase associated disorder known to be susceptible to treatment with compounds of formula III, as construed above, as diagnosed by a second party, likely a physician or other clinician." (Joint Statement at 4.) The reasoning Apotex offers for this construction is that the subject must be known to require such treatment before administration of the disclosed compounds. (See Defs. Opening Br. at 13.) In addition to the arguments advanced in their briefs, Apotex explained at oral argument that the term requires two actors because it includes "in need thereof":

> [T]his goes to a need for multiple actors. First of all, you need the subject. And then you need somebody

> to diagnose the disorder. I don't think the patentee specifically limited this patent to just those people who are able to self-diagnose the disorder themselves, but were meant to open it up to more than just those people. And then, of course, if we're talking about non-human animals, then certainly a dog or cat would not be able to diagnose themselves, and we would need a second actor.

(9-10-12 Transcript at 179, lines 8-16.) Apotex also relies on the specifications of the '746, '875, and '856 Patents for the proposition that a "subject in need thereof" is one suffering from a protein tyrosine kinase-related disorder. (See Defs. Opening Br. at 14.) Apotex argues that construction of the term should be informed by the specifications, which describe the field of the invention and the purpose of the method claimed as being directed to the treatment of protein tyrosine kinase associated disorders, such as immunologic and oncologic disorders. (See id.)

BMS responds to Apotex's arguments regarding "in need thereof" by distinguishing the two cases Apotex cited, neither of which construed similar claim terms to require a second actor for diagnosing purposes. (See Pl. Responsive Br. at 10-11.) Moreover, BMS argues that the only act being performed is "administering" the compounds, and thus only one actor is required. (See id. at 11.)

Apotex, in its response, argues that BMS artificially imports a limitation into the term "subject" that was not intended from the specification. (See Defs. Responsive Br. at 11.) Apotex argues that merely expressing a preference for one kind of subject (animals, most preferably mammalian) is not sufficient to require the Court to limit the universe of potential subjects to that expressed preference. (See id.) The United States Court of Appeals for the Federal Circuit has previously held that statements of preference in the specification are not presumptively definitional. See Liebel-Flarsheim Co. v. Medrad, Inc., 358 F.3d 898, 913 (Fed.Cir. 2004) ("[I]t is improper to read limitations from a preferred embodiment described in the specification—even if it is the only embodiment—into the claims absent a clear indication in the intrinsic record that the patentee intended the claims to be so limited.") (internal citation omitted). At oral argument, however, counsel for Apotex argued that this should be read in the broadest possible manner, unlimited by an expressed preference in the specification.

> MR. BENCHELL: So, what the specification tells us is that the preferred definition for subjects, not the—not subjects, not all subjects, but the preferred definition is, "Subjects for treatment include animals," not just animals, but "include animals."
>
> So, to answer your earlier question, that would include other living beings, whether that be animals, whether that be your single cell amoebas, or whatever.

> . . .
> THE COURT: Do you know whether anything other than an animal can get this—can develop this problem?
> MR. BENCHELL: I do not know.
> THE COURT: No. But I mean it seems to me that if there's no other organism that can develop this problem, it's a moot point.
> MR. BENCHELL: Well, but you can also—I mean, you know, to take it to the extreme, you can take the cancer tumor, and that will continue to grow in a petri dish. You can take those types of organs that can continue to live outside the body.

(9-10-12 Transcript at 177-178.)

The Court has considered the parties' respective arguments, the patent claims, and specification. The Court agrees with the patentee that the intrinsic evidence does not limit the term by requiring multiple actors nor must the field of potential subjects be left open to the wide universe proposed by Apotex. See Liebel-Flarsheim, 358 F.3d at 913. Finally, the Court is unpersuaded by Apotex's argument to broaden the universe of subjects to all living organisms when the intrinsic evidence demonstrates that the drug was intended for those subjects with the targeted disease -- animals, including humans. The Court thus construes the term "a subject in need thereof" as follows:

An animal, including a human, in need thereof.

4. "Wherein the cancer is resistant to treatment by STI-571"

The term appears in claims 9, 10, 12, and 27 of the '875 Patent, which are directed to methods for the treatment of cancer "wherein the cancer is resistant to treatment by STI-571." (See '875 Patent at col. 278, lines 35-40, 60-61; col. 282, line 15.)

BMS proposes that the term be given its ordinary and customary meaning as understood by a person of ordinary skill in the art. (See Pl. Opening Br. at 17.) BMS asks the Court to construe the term to mean: "wherein the cancer [or chronic myelogenous leukemia (CML)] exhibits resistance to treatment by STI-571". (Joint Statement at 23.) BMS argues that this construction comports with the meaning of resistant as defined in the Merriam-Webster's Collegiate® Dictionary: "giving or capable of resistance". (See Pl. Opening Br. at 17.) BMS notes that the '875 Patent discloses that the claimed compounds that are the subject of the patent may be useful "in the treatment of cancers that are sensitive to and resistant to chemotherapeutic agents that target BCR-ABL and c-KIT, such as, for example, Gleevec® (STI-571)." (Id. at 17 (citing Jorgensen Ex. C, col. 28, ll. 26-28).)

Apotex argues that the term should be construed to require both a subject in need of cancer treatment and a second actor who diagnosed the cancer as being resistant to STI-571. (See Defs. Opening Br. at 17.) Apotex argues that the '875 Patent presents a specific objective for the use of the compounds that creates a limitation on subsequent claims: "The compounds of the present invention are also useful in the treatment of cancers that are sensitive to and resistant to chemotherapeutic agents that target BCR-ABL and c-KIT, such as, for example, Gleevec® (STI-571)." (See id. (citing '875 Patent at col. 28, lines 35-38).) Relying on this language in the specification, Apotex argues that the resistance to STI-571 is a limitation necessitating one actor be trained in the diagnosis and treatment of cancer. (See id. at 17-18.)

Apotex also cites two cases for support of this position. (See id. at 17.) In Jansen, the court determined that language in the claim preamble established "the objective of the method, and the body of the claim directs that the method be performed on someone 'in need.' In both cases, the claims' recitation of a patient or a human 'in need' gives life and meaning to the preambles' statement of purpose." Jansen v. Rexall Sundown, Inc., 342 F.3d 1329, 1333 (Fed.Cir. 2003). In Schering, the court was asked to construe the phrase "in need of such

treatment" after "the parties agreed that [the phrase] mean[t] 'one or more therapeutic effects of the type identified in the preamble are required or wanted.'" Schering Corp. v. Glenmark Pharms. Inc., No. 07-1334, 2008 WL 4307189, at *9 (D.N.J. Sept. 16, 2008) (finding the phrase "had intent written into it", such that the words "require" and "wanted" "intimate an intent to use the drug for the purpose it was intended"). Apotex also argues that BMS's proposed definition impermissibly broadens the scope of the claim by changing the term from "is resistant to" to "exhibits resistance". (See Defs. Responsive Br. at 14-15.)

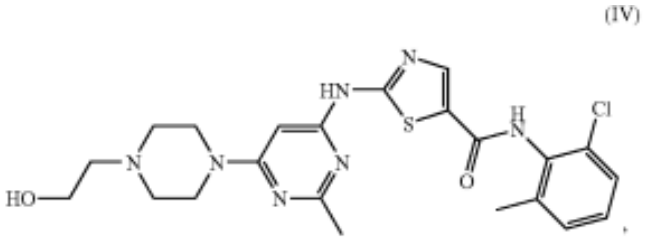
These cases are distinguishable because the specification does not include a purpose-driven declaration for the method claimed as was the case in Jansen; rather the specification notes that the drug can be useful for treatment where the patient is resistant or sensitive to another drug. See Jansen, 342 F.3d at 1333. (See '875 Patent at col. 28, lines 35-38.) Similarly, the parties in Schering agreed to a specific definition that included the words "wanted" and "required", neither of which is present in or analogous to the phrase "wherein the cancer is resistant to treatment by STI-571." See Schering, 2008 WL 4307189, at *9. Accordingly the Court rejects Apotex's argument that the phrase should be construed to require two actors. Moreover, the Court is unpersuaded by Apotex's

arguments regarding the meaning of "is resistant to". Resistance, as BMS noted during oral argument, is not a proposition of duality (entirely resistant or entirely unresistant), but rather presents as a continuum along which patients can exhibit degrees of resistance to treatment. (See 9-10-12 Transcript at 188-89.) Apotex's argument creates a new limitation by defining the term to only include those patients who are completely resistant to STI-571, without any recognition that such resistance may present in degrees of inefficacy in that treatment. (See Defs. Responsive Br. at 15; Pl. Opening Br. at 17; 9-10-12 Transcript at 193-95.)

The Court has considered the parties' respective arguments, the patent claims, the specification and the extrinsic evidence. The Court agrees with the patentee that the term does not require either multiple actors or complete resistance to treatment by STI-571 as proposed by Apotex. The Court thus construes the term "wherein the cancer is resistant to treatment by STI-571" as follows:

Wherein the cancer [or chronic myelogenous leukemia (CML)] exhibits resistance to treatment by STI-571.

B. Construction of the '725 Patent

1. "Crystalline monohydrate of the compound of formula (IV)  **"**

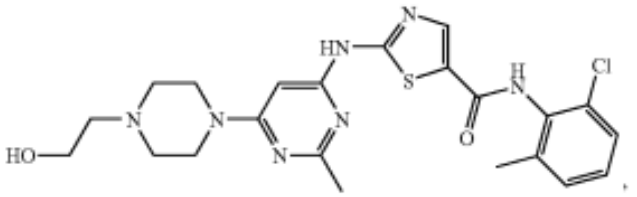
The term appears in claims 1, 3, and 12 of the '725 Patent, which are directed to crystalline monohydrate compounds of formula IV. (See, e.g., '725 Patent at col. 48, lines 48-60.)

BMS proposes that the term be read to comport with its plain meaning as understood by a person of ordinary skill in the art, namely "the monohydrate of the compound of formula IV in a crystalline form." (Joint Statement at 33.) BMS finds support for this argument in the specification, which provides an example of the preparation of a crystalline monohydrate in Example 8. (See Pl. Opening Br. at 18.) A monohydrate, BMS argues, means "a compound containing one molecule of water." (See id. (citing The American Heritage® Dictionary 1137 (4th ed. 2000)).)

Apotex argues that "crystalline monohydrate" is only a general term, given meaning by the intrinsic evidence of specified results achieved upon analytical testing. (See Defs. Opening Br. at 18.) Apotex would have the Court construe the

term to mean "[r]aw material produced by process conditions presented in the specifications, with a particular arrangement

(IV)



of the following compound:

in three dimensional space that has a certain degree of long range order, with a 1:1 molar arrangement of water to compound formally associated in a unit crystal cell lattice." (Joint Statement at 33.) Apotex argues that a "crystalline monohydrate" is a general term encompassing multiple polymorphous versions of crystal lattice frameworks. (See Defs. Opening Br. at 19-20.) These different forms are identifiable only through specific testing and observational means, and therefore, Apotex argues, the claim should be limited to the specific crystalline monohydrate described in the results achieved through analytical testing. (See id. at 19.)

Apotex also argues, based on a specification for an earlier application, that the '725 Patent was not originally intended to describe crystalline monohydrates. (See id. at 20.) Rather, the "'invention relates to process for preparing compounds' of a general formula, . . . [and the phrase] 'and crystalline forms

thereof' was a later addition to the '725 patent's application, which was originally filed as a patent application directed towards only processes for preparing compounds." (Id.) Apotex places great weight on the precise methodologies for preparation and testing that are mentioned in the '725 Patent, arguing:

> the '725 patent is quite particular about the methodologies that can be used to prepare the "crystalline monohydrate of the compound of formula (IV)." . . . It is clear to a person of ordinary skill in the art reading the specification that the particular processes that BMS originally sought to patent were what prompted the monohydrate crystal formulation.

(Id. at 20-21 (internal citations omitted).) Apotex argues that the invention must be "a stand-alone, raw material substance, and not a mixture" for three reasons: (1) the only mixtures mentioned in the '725 Patent are described in other dependent claims and are made up of the drug with excipients in pharmaceutical composition; (2) the specification states that "[t]he present invention also provides using the compounds obtained with the inventive process to further prepare pharmaceutical compositions"; and (3) the results achieved through analytical testing will only be "substantially" in conformance with the figures listed in the claims if the analytical tests are conducted on raw material samples. (See id. at 21.) Apotex cites Abbott Labs. as support for limiting a

claim to the product when a specific crystal was the only product capable of achieving the analytical test results set forth in the specification and claims of the patent. Abbott Labs. v. Sandoz, Inc., 566 F.3d 1282 (Fed.Cir. 2009).

Apotex further argues under the prosecution history that BMS should be limited to only those crystals that are produced by the specification's procedures. (See Defs. Opening Br. at 22.) During prosecution, the PTO Examiner rejected claims for the crystalline monohydrate on the basis of prior art in the field that would lead a person of ordinary skill in the art to expect that compounds in the class would form hydrates and solvates. (See id.) When BMS responded that the prior art did not disclose a monohydrate of the compound of formula IV in a crystalline form, the PTO in turn accepted the detailed structural information and lack-of-expectation assertion as entitling BMS to only "the crystalline forms that are adequately described in the specification and [not granting BMS] a generic crystalline claim." (See id. (citing Shannon Decl., Ex. G, '725 patent PH, 3/3/08 Office Action, at 4 (APO(Das)016420)).)

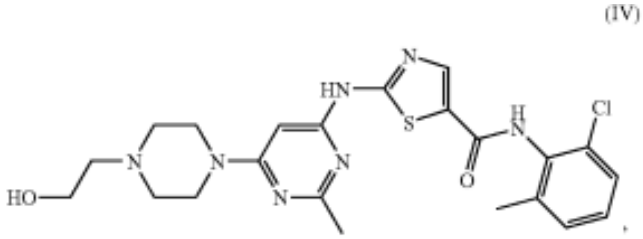
BMS responds that Phillips requires courts to construe claim terms in light of the patent as a whole, including its specification, and that the specification to be examined is the one in the issued patent, not earlier versions. (See Pl.

Responsive Br. at 13 n.3 (citing Sun Pharm. Indus., Ltd. v. Eli Lilly & Co., 611 F. 3d 1381, 1388 (Fed.Cir. 2010) (quoting Phillips, 415 F.3d at 1316)).) Moreover, BMS notes that Apotex points only to the testimony of its expert for support that the term should be construed to mean a raw material that resulted from the process conditions exemplified in Example 8. (See id. at 13.) BMS highlights several concerns with the expert's opinion, notably his conclusion's lack of foundation in the intrinsic evidence, his failure to conduct experimentation to produce the monohydrate through other procedures, and several contradictory statements when his conclusion is compared to the '725 Patent as a whole. (See id. at 14.) BMS points out that the same expert conceded the term "raw material" does not appear in any of the claims of the '725 Patent, nor do the claims expressly or implicitly limit the invention to the process conditions. (See id.) With respect to Apotex's reliance on Abbott Labs., BMS responds that the Court of Appeals for the Federal Circuit has already rejected that argument: "this court expressly rejected the contention that if a patent describes only a single embodiment, the claims of the patent must be construed as being limited to that embodiment." Abbott Labs., 566 F.3d at 1290 (internal citation omitted). Moreover, BMS distinguishes Abbott Labs. because the district court there

rested the decision to limit the patent on the fact that "the rest of the intrinsic evidence, including the prosecution history and the priority [] application, evince[d] a clear intention to limit the '507 patent to Crystal A as defined by the seven PXRD peaks in the specification and in claim 1." Id. (See Pl. Responsive Br. at 14-15.)

The Court has considered the parties' respective arguments, the patent claims, the specification, the prosecution history and the expert evidence. The Court agrees with the patentee that the term should not be limited by the example described in the specification or by the analytical test results used to specify structural information about the crystalline monohydrate. The Court thus construes the term "Crystalline monohydrate of the compound of formula

(IV)



" as follows:

The monohydrate of the compound of formula (IV) in a crystalline form.

2. "Which is characterized by an x-ray powder diffraction pattern substantially in accordance with that shown in FIG. 1"

The term appears in claim 1 of the '725 Patent. (See '725 Patent at col. 48, lines 62-63.) BMS proposes a construction as follows: "which is characterized by an x-ray powder diffraction pattern that is substantially identical to those shown in FIG. 1 taking into account variations due to measurement errors and dependent upon the measurement conditions employed, but not taking into account the exact order of intensity of the peaks." (Joint Statement at 34.) BMS also notes that it considers "the ability to ascertain substantial identities of X-ray diffraction patterns [to be] within the purview of one of ordinary skill in the art." (Id.) BMS points to statements in the specification that "[a]ny crystal forms that provide X-ray diffraction patterns substantially identical to those disclosed in the accompanying Figures fall within the scope of the present invention. The ability to ascertain substantial identities of X-ray diffraction patterns is within the purview of one of ordinary skill in the art." ('725 Patent at col. 42, lines 8-13.) Further, the specification discloses:

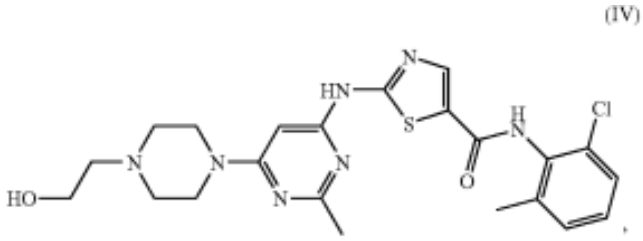
> One of ordinary skill in the art will appreciate that an X-ray diffraction pattern may be obtained with a measurement error that is dependent upon the measurement conditions employed. In particular, it is generally known that intensities in an X-ray diffraction pattern may fluctuate depending upon

> measurement conditions employed. It should be further understood that relative intensities may also vary depending upon experimental conditions, and accordingly, the exact order of intensity should not be taken into account. Additionally, a measurement error of diffraction angle for a conventional X-ray diffraction pattern is typically about 5% or less, and such degree of measurement error should be taken into account as pertaining to the aforementioned diffraction angles. Consequently, it is to be understood that the crystal forms of the instant invention are not limited to the crystal forms that provide X-ray diffraction patterns completely identical to the X-ray diffraction patterns depicted in the accompanying Figures disclosed herein.

(Id. at col. 41, line 58 to col. 42, line 8.) BMS argues that its construction accounts for the variations in test results that a person of ordinary skill in the art would recognize are normally attributable to measurement errors or conditions. (See Pl. Opening Br. at 20.) The Court of Appeals for the Federal Circuit has previously deemed the term "substantially" a "descriptive term[] commonly used in patent claims to avoid a strict numerical boundary to the specified parameter". See Playtex Prods., Inc. v. Procter & Gamble Co., 400 F.3d 901, 907 (Fed.Cir. 2005). Additionally, BMS argues that "the patent teach[es] that peak intensities may fluctuate and the exact order of intensity of the peaks should not be considered in comparing X-ray diffraction patterns." (Pl. Opening Br. at 20 (citing '725 Patent at col. 41, line 58 to col. 42, line 13).)

Apotex proposes the following construction: "[t]he product being characterized much match the x-ray powder diffraction pattern presented in FIG. 1 of the patent specification, and further do so in such a way so as to uniquely identify the referenced '[c]rystalline monohydrate of the compound of formula

(IV)



." (Joint Statement at 34.) Apotex argues that BMS's definition of "substantially" vitiates the term and impermissibly broadens the scope of the claim beyond the "one specific 'crystalline monohydrate' and . . . XRPD 'fingerprint' shown in Figure 1 of the '725 patent" that BMS chose to claim. (Defs. Opening Br. at 25.) To oppose BMS's suggestion that the exact order of peak intensity should not be taken into account, Apotex relies on an expert to argue that "even slight differences in an XRPD pattern can result in an inability to uniquely identify the substance being considered." (Id. at 26.) Further, Apotex argues that an XRPD pattern that was "substantially identical" to those in Figure 1 would leave a person of ordinary skill in the art without confidence that the

product tested is in fact the patented "[c]rystalline monohydrate of the compound of formula (IV)." (Id.)

BMS responds to Apotex's argument by pointing out that Apotex can find no intrinsic evidence to support the construction that "the product being characterized must match the x-ray powder diffraction pattern presented in FIG. 1 of the patent specification". (Pl. Responsive Br. at 16.) BMS also points out that Apotex's expert contradicts this definition by testifying that "substantially in accordance" does not mean "must match" but rather "matches well". (See id.) Additionally, the expert recognizes that XRPD results can have measurement errors and can result in two x-ray diffraction patterns having different intensities but yet representing the same crystalline material. (See id. at 17.) Apotex in its response renews its arguments regarding the linguistic ambiguities inherent in the terms "substantially in accordance" or "substantially identical." (See Defs. Responsive Br. at 21-24.)

The Court has considered the parties' respective arguments, the patent claims, the specification and the expert evidence. The Court agrees with the patentee that the term "substantially in accordance" should not be construed so strictly as to unduly narrow the scope of the claim. Furthermore, the Court rejects

the extrinsic testimonial evidence of Apotex's expert in favor of the teachings of the patent concerning importance of peak intensities. The Court thus construes the term "which is characterized by an x-ray powder diffraction pattern substantially in accordance with that shown in FIG. 1" as follows:

Which is characterized by an x-ray powder diffraction pattern that is substantially identical to those shown in FIG. 1 taking into account variations due to measurement errors and dependent upon the measurement conditions employed, but not taking into account the exact order of intensity of the peaks.

3. "The compound of claim 1" or "The compound of claim 3" or "A process for preparing the compound of claim 3" or "The compound of claim 9" or "the compound of claim 12"

These terms appear in claims 2, 4-11, and 13-16 of the '725 Patent, which depend directly or indirectly from claims 1, 3, or 12. (See, e.g., '725 Patent, col. 49, lines 39-40.) The parties' arguments and constructions of the terms will be separately treated by the Court in analysis and construction.

a. "The compound of claim 1" or "The compound of claim 3" or "The compound of claim 9" or "the compound of claim 12"

BMS proposes that the term used in claims 2, 4, 5, 8-11, and 13-16 be given its plain meaning as understood by a person of ordinary skill in the art, namely, "the crystalline monohydrate of the compound of formula (IV)." (Joint Statement at 35.) Apotex would have the term in claim 2 mean: "[t]he compound defined by claim 1, including all limitations of claim 1." (Id.) As used in claims 4, 5, 8-10, and 13, Apotex proposes the claim be construed as "[t]he compound that is identified and defined as such in claim 3; [which in turn is identified in claim 9]; this construction renders claim [4,5, 8, 9, 10] invalid for improper dependency." (Joint Statement at 39 (noting also that "[t]o the extent the claim is construed as limited to a particular crystal form, the claim is not enabled and/or not infringed because the crystal form no longer exists if it is to engage in any therapeutic activity."), 41, 43, 46, 47, 50.) As used in claims 14-16, Apotex requests that the Court construe the term to mean "the compound that is identified and defined as such in claim [9, 12]; this construction renders claim [14, 15, 16] invalid for improper dependency." (Joint Statement at 50, 51, 52.)

BMS argues succinctly that the Court should construe the term to mean "the plain and ordinary meaning of the phrase as understood by one of skill in the art based on the specification, namely the monohydrate of the compound of formula IV in a crystalline form." (Pl. Opening Br. at 21.) As an illustrative example, BMS points to claim 2, which recites a compound of claim 1 characterized by a differential scanning calorimetry thermogram substantially in accordance with FIG. 2. (See '725 Patent at col. 48, lines 64-67.) BMS further notes that FIG. 2 displays "a DSC and TGA of 'the monohydrate of the compound of Formula (IV).'" Thus, BMS argues that, when the specification and claims are read in context, the term means "the monohydrate of the compound of formula IV in a crystalline form." (Pl. Opening Br. at 22 (citing Phillips, 415 F.3d at 1314; Pause Tech. LLC v. TiVo, Inc., 419 F.3d 1326, 1331 (Fed.Cir. 2005) ("proper claim construction . . . demands interpretation of the entire claim in context, not a single element in isolation.")).) BMS finally argues that Apotex's proposed constructions do not qualify as constructions of claims, but rather as "arguments concerning the validity of the claims", finding no support in either the claim language or the patent specification. (See Pl. Opening Br. at 22.)

Apotex argues that the specification teaches there is a difference between "crystalline monohydrate" and a "compound": "The compound of formula (IV) . . . is an inhibitor of SRC/ABL and is useful in the treatment of oncological diseases." ('725 Patent at col. 1, lines 51-65.) In another section, the specification notes that "another aspect" of the invention is "crystalline forms of the compound of formula (IV)." (Id. at col. 4, lines 55-56.) Apotex argues that, by distinguishing between the crystalline form and the compound, the specification teaches that "a compound of Formula IV can exist in multiple iterations (such as in solution) in a manner distinct from the monohydrate structure (since a monohydrate structure is a creature of the solid phase, not the liquid phase)." (Defs. Opening Br. at 36.)

The Court has considered the parties' respective arguments, the patent claims, and the specification. The Court agrees with the patentee that the term "the compound of claim [1, 3, 9, 12]" is not insolubly ambiguous so as to render the claim invalid. Furthermore, the Court finds that a person of ordinary skill in the art could rely on the teachings of the patent as a whole concerning the meaning of the terms. From reading the '725 Patent as a whole, a person of ordinary skill would understand that the subject of these claims is properly the crystalline

monohydrate. The Court thus construes the term "[t]he compound of claim 1" or "[t]he compound of claim 3" or "[t]he compound of claim 9" or "the compound of claim 12" as follows:

The monohydrate of the compound of formula (IV) in a crystalline form.

b. "A process for preparing the compound of claim 3"

BMS proposes the term as used in claims 6 and 7 be given its plain meaning as understood by a person of ordinary skill in the art: "a process for preparing the crystalline monohydrate of the compound of formula (IV)." (Joint Statement at 40.) BMS did not differentiate between this term and those immediately preceding so, with respect to this term, BMS made no separate arguments in its opening papers. (See Pl. Opening Br. at 21.)

Apotex argues that the term should be construed so that the process addressed "must occur in the United States for preparing." (Joint Statement at 40.) Apotex also argues that the term is vague and indefinite in the context of the claim. (See id.) Apotex notes that these claims are directed to "'[a] process for preparing the compound of claim 3' comprising heating, dissolving, and crystallizing steps and specifying various parameters." (Defs. Opening Br. at 34.) Relying on 35

U.S.C. § 271(a), Apotex argues that, with respect to infringement of a process claim, any allegedly infringing act must occur inside the United States in order to support a finding of infringement. (See id. at 35.)

BMS rejects Apotex's argument in reply, noting that Apotex has not offered a construction, but rather argued about where any infringement may occur. (See Pl. Responsive Br. at 26.) BMS notes that there is no intrinsic evidence to suggest the process was restricted to the United States, nor does case law preclude a patented product made outside the United States, but later imported into the country, from potentially infringing a patent. (See id.)

The Court has considered the parties' respective arguments, the patent claims and the specification. The Court agrees with the patentee that neither case law nor the intrinsic evidence of the patents require the term "[a] process for preparing the compound of claim 3" to signify that the "process" occur in the United States. The Court thus construes the term "[a] process for preparing the compound of claim 3" as follows:

A process for preparing the crystalline monohydrate of the compound of formula (IV).

4. "Which is characterized by differential scanning calorimetry thermogram and a thermogravimetric analysis substantially in accordance with that shown in FIG. 2"; "[being further] characterized by a differential scanning calorimetry having a broad peak between approximately 95° C and 130° C"; "wherein the differential scanning calorimetry further has a peak at approximately 287° C"

Although the parties separate the terms in the Joint Statement, Apotex has addressed the three terms simultaneously and BMS too overlaps its proposed constructions. (See Joint Statement at 36, 44, 48; Pl. Opening Br. at 22, 27, 30; Defs. Opening Br. at 30.) Accordingly the Court will set forth the proposed constructions separately but provide the parties' arguments and the Court's construction of the terms together.

a. "Which is characterized by differential scanning calorimetry thermogram and a thermogravimetric analysis substantially in accordance with that shown in FIG. 2"

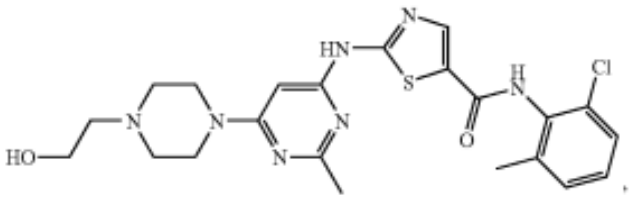
The term "[w]hich is characterized by differential scanning calorimetry thermogram and a thermogravimetric analysis substantially in accordance with that shown in FIG. 2" appears in claim 2 of the '725 Patent, which depends directly on claim 1. (See '725 Patent, col. 48, line 64.)

BMS proposes that the term be construed to mean the following:

> Which is characterized by differential scanning calorimetry thermogram and thermogravimetric analysis

> patterns that are substantially identical to those shown in FIG. 2, having one peak at approximately 287° C and one broad peak between approximately 95° C and approximately 130° C. The ability to ascertain substantial identities of patterns is within the purview of one of ordinary skill in the art.

(Joint Statement at 36.) Apotex proposes:

> The product being characterized must match both the differential scanning calorimetry thermogram and the thermogravimetric results presented in FIG. 2 of the patent specification, and further do so in such a way as to uniquely identify the referenced "[c]rystalline monohydrate of the compound of formula (IV)
>
> (IV)
>
> 
>
>
> . . . ."
>
> At least the phrase "differential scanning calorimetry thermogram . . . in accordance with that shown in FIG. 2" is indefinite owing to the failure, in the patent specification to disclose the methodology for testing. (E.g., open pan, first run/second run).

(Id.)

b. "[Being further] characterized by a differential scanning calorimetry having a broad peak between approximately 95° C and 130° C"

The term "[being further] characterized by a differential scanning calorimetry having a broad peak between approximately 95° C and 130° C" appears in claims 9 and 12 of the '725 Patent. (See id. at col. 50, lines 1-3, 25-26.)

BMS proposes the term be construed to mean: "being further characterized by a differential scanning calorimetry having a broad peak between about 95° C and about 130° C. This peak can be variable but corresponds to the loss of one water of hydration on thermogravimetric analysis." (Joint Statement at 44.) Apotex's proposed construction is as follows:

> The product being characterized must match the stated results.
> The term "broad peak" is vague and indefinite. The term "peak" is not routinely used in the context of analyzing differential scanning calorimetry data. To the extent the term is intended to refer to endotherms or exotherms that can appear in a DSC trace, the claim language is indefinite and/or non-enabled.
> "Approximately" is indefinite in the context of the claims.
> At least the phrase "differential scanning calorimetry" is indefinite owing to the failure to disclose the methodology for testing. (E.g., open pan, first run/second run).

(Id.)

c. "Wherein the differential scanning calorimetry further has a peak at approximately 287° C"

The term "wherein the differential scanning calorimetry further has a peak at approximately 287° C" appears in claim 11 of the '725 Patent. (See id. at col. 50, lines 10-11.)

BMS proposes the term be construed to mean "characterized by differential scanning calorimetry with a peak located at about 287° C which corresponds to the melt of the dehydrated

form of the compound of formula (IV)." (Joint Statement at 48.)

Apotex proposes the term be construed as follows:

> The product being characterized must match the stated results.
> The term "broad peak" is vague and indefinite. The term "peak" is not routinely used in the context of analyzing differential scanning calorimetry data. To the extent the term is intended to refer to endotherms or exotherms that can appear in a DSC trace, the claim language is indefinite and/or non-enabled.
> "Approximately" is indefinite in the context of the claims.
> At least the phrase "differential scanning calorimetry" is indefinite owing to the failure to disclose the methodology for testing. (E.g., open pan, first run/second run).

(Id.)

d. Arguments and Construction

BMS argues that its proposed constructions of the terms are supported by the specification as it would be understood by a person of ordinary skill in the art. (See Pl. Opening Br. at 23.) The '725 Patent includes language describing the graphical depiction in FIG. 2, which mirrors BMS's proposed construction for the terms:

> The monohydrate of the compound of formula (IV) is represented by the DSC as shown in FIG. 2. The DSC is characterized by a broad peak between approximately 95° C. and 130° C. This peak is broad and variable and corresponds to the loss of one water of hydration as seen in the TGA graph. The DSC also has a characteristic peak at approximately 287° C. which corresponds to the melt of the dehydrated form of the compound of formula (IV).

('725 Patent at col. 45, lines 15-22.) BMS also notes that one of ordinary skill in the art would recognize that inherent measurement errors and conditions may cause variations, and thus would take those factors into account when ascertaining the substantial identities of differential scanning calorimetry or thermogravimetric analysis patterns. (See Pl. Opening Br. at 23.) Finally, BMS argues that Apotex's construction would improperly write "substantially in accordance" out of the claim in contravention of the plain language of the claim and the teachings of the specification. See Bicon, Inc. v. Straumann Co., 441 F.3d 945, 951-52 (Fed.Cir. 2006).

Apotex argues that one ordinarily skilled in the art would be unable to understand the meaning of the terms. (See Defs. Opening Br. at 30.) Apotex makes four arguments regarding confusion: (1) one skilled in the art would be confused about how to perform the differential scanning calorimetry test without the patent teaching the methodology for conditions and related variables; (2) "substantially in accordance" fails to sever the claims from the particularly described monohydrate crystal as set forth in the specification, even if BMS wants to broaden the scope of the claim (to also encompass other hydrates, compounds or excipients); (3) a person of ordinary skill in the art would not describe differential scanning

calorimetry data outputs with the term "peak", giving it no "plain meaning" in this context; and (4) words of degree like "broad peak", "approximately 95° C and 130° C" or "approximately 287° C" inhibit the guidance or standards that a person of ordinary skill in the art would need to properly quantify the breadth of the peak in differential scanning calorimetry patterns. (See id. at 31-32.)

BMS responds that Apotex's assertions of insoluble ambiguity are wrong because: (1) sufficient instructions were provided for one of ordinary skill in the art to replicate the experimental conditions used by the inventors (see, e.g., '725 Patent at col. 43, lines 1-22.); (2) Apotex is merely abandoning a construction of the term in claim 2 that was unsupported by its expert, who stated that "substantially in accordance" does not mean "must match"; (3) the term does not broaden the scope of the claim to other hydrates, compounds, or excipients because it explicitly limits itself to "the crystalline monohydrate of the compound of formula (IV)"; (4) "peak" is known and used in the art, as demonstrated by the testimony of the experts for both BMS and Apotex; and (5) Apotex's own expert understood that "broad peak between approximately 95° C and 130° C" corresponded to the loss of one water of hydration and that errors associated with testing could make the use of "approximately" appropriate

in this context. (See Pl. Responsive Br. at 21-23.) Apotex, in response and at oral argument, argues that the insoluble ambiguity of the claims would prevent one of ordinary skill in the art from understanding the claim. (See Defs. Responsive Br. at 26-28; 9-10-12 Transcript at 67, line 5 to 70, line 17.)

The Court has considered the parties' respective arguments, the patent claims, the specification, and the experts' testimonial evidence. The Court agrees with the patentee that the ability to ascertain substantial identities of patterns is within the purview of one of ordinary skill in the art and that the specification's instructions disclose sufficient guidance to permit replication of the methodology. The Court also finds that the term "substantially in accordance" does not require that analysis of the product being characterized must identically match the results as stated in the figure. The Court thus construes the terms "[w]hich is characterized by differential scanning calorimetry thermogram and a thermogravimetric analysis substantially in accordance with that shown in FIG. 2", "[being further] characterized by a differential scanning calorimetry having a broad peak between approximately 95° C and 130° C" and "wherein the differential scanning calorimetry further has a peak at approximately 287° C" as follows:

Which is characterized by differential scanning calorimetry thermogram and thermogravimetric analysis patterns that are substantially identical to those shown in FIG. 2, having one peak at approximately 287° C and one broad peak between approximately 95° C and approximately 130° C.

Being further characterized by a differential scanning calorimetry having a broad peak between about 95° C and about 130° C.

Characterized by differential scanning calorimetry with a peak located at about 287° C which corresponds to the melt of the dehydrated form of the compound of formula (IV).

5. **"[W]hich is characterized by an x-ray powder diffraction pattern (CuK_α λ=1.5418 Å at a temperature of about 23°C.) comprising four or more 2θ values selected from the group consisting of 18.0±0.2, 18.4±0.2, 19.2±0.2, 19.6±0.2, 21.2±0.2, 24.5±0.2, 25.9±0.2, and 28.0±0.2"**

The term appears in claim 3 of the '725 Patent. (See '725 Patent, col. 49, lines 14-18.)

BMS proposes that the term be given its plain meaning as understood by one of ordinary skill in the art. Accordingly, BMS would have the term stand as is. (See Joint Statement at 38.) Apotex would have the Court construe the term as follows:

> The product being characterized must uniquely identify the referenced "[c]rystalline monohydrate of the compound of formula (IV)"

> And generate an x-ray powder diffraction pattern using the methodology provided (CuKα λ=1.5418 Å at a temperature of about 23°C).
> The term "2θ values" is vague and indefinite.
> "selected from the group consisting of" is Markush language, but in the context of the claims is vague and indefinite; [sic]
> To the extent variance is permitted, it is not supported by the claims; is indefinite and not supported by the written description; and violates the Markush concept.

(Id.)

BMS argues that the term is unambiguous and well-understood by those of ordinary skill in the art as written. (See Pl. Opening Br. at 24.) BMS contrasts its suggested definition with that proposed by Apotex and notes that Apotex seeks to import limitations into the term that are not supported by the specification or any other intrinsic evidence. (See id. at 24-25.)

Apotex argues that this claim can only cover "one unique type of crystal . . . produced according to the specification procedures." (Defs. Opening Br. at 27.) This claimed crystal must have all the peaks noted in the claim and many others, making the language in the term redundant and perhaps even excluding the very crystal supposedly claimed under the patent. (See id. at 27-28.) Apotex also argues that this allows BMS to claim other materials with some of the peaks described, but not all that the crystal would have. (See id. at 28.) Finally,

Apotex argues that the variance of "±0.2" is unsupported by the specification. (See id.)

The Court has considered the parties' respective arguments, the patent claims, the specification, and the experts' testimonial evidence. The Court agrees with the patentee that the ability to ascertain substantial identities of patterns is within the purview of one of ordinary skill in the art and that the instructions provided in the specification are sufficient guidance to permit replication of the methodology. The Court also finds that the term "substantially in accordance" does not require that analysis of the product being characterized must identically match the results as stated in the figure. The Court is unpersuaded by Apotex's argument against the "±0.2" variance, noting that Apotex does not offer the testimony of an expert to counter BMS's expert's contention that the peaks were tethered to the monohydrate in the specification and that such variances were commonly used by persons of ordinary skill in the art. The Court thus construes the term "[w]hich is characterized by differential scanning calorimetry thermogram and a thermogravimetric analysis substantially in accordance with that shown in FIG. 2" as follows:

Which is characterized by an x-ray powder diffraction pattern taken with CuK_{α} λ=1.5418 Å at a temperature of about

23°C, having at least four 20 values selected from the group consisting of 18.0±0.2, 18.4±0.2, 19.2±0.2, 19.6±0.2, 21.2±0.2, 24.5±0.2, 25.9±0.2, and 28.0±0.2.

6. "[C]haracterized by unit cell parameters approximately equal to the following dimensions: Cell dimensions: a(Å)=13.8632(7); b(Å)=9.3307(3); c(Å)=38.390(2); Volume=4965.9(4) Å^3 Space group Pbca Molecules/unit cell 8 Density (calculated) (g/cm^3) 1.354"

The term appears in claim 5 of the '725 Patent. (See '725 Patent at col. 49, lines 23-32.)

BMS proposes that the term be given its plain meaning as understood by one of ordinary skill in the art. (See Joint Statement at 40; Pl. Opening Br. at 25.) Apotex raised indefiniteness and written description invalidity defenses to this claim language, but fails to offer the Court a proposed definition: "Apotex respectfully submits that this language is insolubly ambiguous, unsupported and not capable of being construed." (Defs. Opening Br. at 29 n.9, 30; see Joint Statement at 40.) Apotex argues that the term is too precisely rendered to refer to "anything but a specially-grown single crystal; there is no standard for 'approximately equal.'" (Defs. Opening Br. at 29.)

BMS responds that the term "approximately equal" is unambiguous and well-understood by those of ordinary skill in

the art as written. (See Pl. Opening Br. at 20.) BMS contrasts testimony from Apotex's expert about the confusion from "approximately equal" with the same expert's suggestion for a meaningful substitution: "approximately the same". (See id. at 20-21.) BMS also rebuts Apotex's argument that the unit cell parameters listed in the claim could not be achieved if the compound was in powder form, as would be required for other elements of the claim. (See id.) Apotex's expert testified that the tests in the claim could produce the results as written, which undermines the argument that the language is ambiguous because it would not be understood by a person of ordinary skill in the art. (See id.) BMS asserts that these semantics-based or purely attorney arguments cannot overcome the plain language of the claim. (See id.)

Apotex renews its arguments regarding the different preparations of the compound for the tests and indefiniteness of the term in its response. (See Defs. Responsive Br. at 25-26.) BMS cited, inter alia, Merck & Co. v. Teva Pharm. U.S.A., Inc., 395 F.3d 1364, 1372 (Fed.Cir. 2005), where the court had construed "approximately" to mean "about". Apotex argues that the parties there had stipulated to a definition of the term and that the case is less relevant than Amgen, which invalidated a claim containing the phrase "at least about 160,000" for

indefinite limitation. See Amgen, Inc. v. Chugai Pharm. Co., 927 F.2d 1200, 1218 (Fed.Cir. 1991). (See Defs. Responsive Br. at 26.) The Court is unpersuaded by Apotex's reading of the case cited. In Amgen, the court determined that the claim was invalid based on, inter alia, the prosecution history of the patent in question:

> When the examiner noticed this disclosure late in the prosecution, he rejected the '195 claims with a specific activity limitation of "at least 120,000" as anticipated by the Miyake et al. disclosure. It was only after the "at least 120,000" claims were cancelled that [the patentee] submitted the "at least about 160,000" claim language.
>
> The [district] court found the "addition of the word 'about' seems to constitute an effort to recapture . . . a mean activity somewhere between 120,000, which the patent examiner found was anticipated by the prior art, and [the] 160,000 IU/AU" claims which were previously allowed. Because "the term 'about' 160,000 gives no hint as to which mean value between the Miyake et al. value of 128,620 and the mean specific activity level of 160,000 constitutes infringement," the court held the "at least about" claims to be invalid for indefiniteness. This holding was further supported by the fact that nothing in the specification, prosecution history, or prior art provides any indication as to what range of specific activity is covered by the term "about," and by the fact that no expert testified as to a definite meaning for the term in the context of the prior art. In his testimony, Fritsch tried to define "about" 160,000, but he could only say that while "somewhere between 155[,000] might fit within that number," he had not "given a lot of direct considerations to that. . . ."

Amgen, 927 F.2d at 1217-18.

The Court has considered the parties' respective arguments, the patent claim, the specification, and the experts' testimonial evidence. The Court agrees with the patentee that "approximately equal" is unambiguous and well-understood by those of ordinary skill in the art, and that the instructions provided in the specification provide sufficient guidance to permit an expert to reproduce the results specified in the term. The Court thus construes the term "characterized by unit cell parameters approximately equal to the following dimensions:

Cell dimensions: a(Å)=13.8632(7); b(Å)=9.3307(3); c(Å)=38.390(2);

Volume=4965.9(4) $Å^3$

Space group Pbca

Molecules/unit cell 8

Density (calculated) (g/cm^3) 1.354" as follows:

"[C]haracterized by unit cell parameters approximately equal to the following dimensions:

Cell dimensions: a(Å)=13.8632(7); b(Å)=9.3307(3); c(Å)=38.390(2);

Volume=4965.9(4) $Å^3$

Space group Pbca

Molecules/unit cell 8

Density (calculated) (g/cm^3) 1.354"

7. "Wherein the compound is substantially pure"

The term appears in claims 8, 15, and 16 of the '725 Patent, which depend directly or indirectly on either claim 3 or 12. (See, e.g., '725 Patent, col. 48, line 64.)

BMS proposes that the term be construed to mean: "[t]he compound itself having a purity greater than 90 percent. The 'substantially pure' compound may be employed in pharmaceutical compositions to which other desired components are added, for example excipients, carriers, or active chemical entities of different molecular structure." (Joint Statement at 42.) Apotex contends that the term is indefinite, particularly in light of the claim language. (Id.)

BMS argues that the language of the patent specification provides the definition of this term: "[t]he present invention describes crystalline forms of the compound of formula (IV) in substantially pure form. As used herein, 'substantially pure' means a compound having a purity greater than 90 percent, including 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, and 100 percent." ('725 Patent at col. 15, lines 26-30.) The specification further describes an example of a crystalline form of the compound of formula (IV) as being "substantially pure" when it has "a purity greater than 90 percent, where the remaining less than 10 percent of material comprises other

form(s) of the compound of the formula (IV), and/or reaction and/or processing impurities arising from its preparation." (Id. at col. 15, lines 28-40.) BMS argues that the intrinsic evidence of the terms meaning should control the Court's construction. (See Pl. Opening Br. at 26-27.)

Apotex argues, based on Stedman's® Medical Dictionary, that a compound is "a substance formed by the covalent or electrostatic union of two or more elements, generally differing entirely in physical characteristics from any of its components." (Defs. Opening Br. at 24.) Thus, Apotex argues, a compound structure cannot have degrees of purity because its identity will be completely dictated by the precise relative ratios of its individual components. (See id.) Moreover, Apotex argues that the term is too indefinite to provide meaningful guidance to one of ordinary skill in the art because it fails to provide the exact nature of the percentage, purity not being an element or known compound of which the exact presence can be calculated. (See id.) Hence, without an indication that the patent inventors intended purity by weight percent, volume percent, or molar percent, the missing units of purity prevent one of ordinary skill the art from understanding this term. (See id. at 23-24.)

BMS counters that Apotex's expert understood the meaning of the term, and that he testified that a person of ordinary skill in the art could understand what the term indicated in the full context of the patent. (See Pl. Responsive Br. at 15.) Additionally, BMS's expert indicated that, taken as a whole, "the '725 patent would have taught one of ordinary skill in the art that the purity of the crystalline monohydrate of the compound of formula (IV) [should] be measured by weight percent." (See id.; see also dkt. entry no. 67, Supp. Decl. of Jerry Atwood at 2-3.) Finally, BMS argues that the use of terms such as "pure" and "substantially pure" is recognized and supported by case law. (See id. at 15-16 (citing cases).)

Apotex opposes BMS's constructions with renewed arguments that the patent does not define "substantially pure" clearly enough to avoid invalidation for indefiniteness. (See Defs. Responsive Br. at 19-21.)

The Court has considered the parties' respective arguments, the patent claims, the specification, and the experts' testimonial evidence. The Court agrees with the patentee that the instructions in the specification provide sufficient guidance to permit one with ordinary skill in the art to determine whether a substance is "substantially pure". The Court agrees with the patentee that a "substantially pure"

sample of the compound may contain a small amount of material made up of the compound, but which is present in a different form from the crystalline form of the monohydrate, or which is derived from processing or reaction impurities. Moreover, the "substantially pure" compound may be employed in pharmaceutical compositions to which other desired components are added, e.g., excipients, carriers, or active chemical entities of different molecular structure. The Court thus construes the term "wherein the compound is substantially pure" as follows:

"The compound itself having a purity greater than 90 percent."

8. "[W]hich corresponds to the loss of one water of hydration on thermogravimetric analysis"

The term appears in claims 9 and 12 of the '725 Patent. (See, e.g., '725 Patent, col. 50, lines 3-5.)

BMS proposes that the term be construed to mean "which corresponds to a weight loss attributable to one water of hydration on thermogravimetric analysis." (Joint Statement at 45.) Apotex requests that the Court find the term "makes no sense in context, because a 'compound' does not lose water." (Id.) If the Court does not find the language "internally contradictory," Apotex asks the Court to recognize that "the

language out of context would indicate that there is a peak in the DSC that must correspond and otherwise perfectly align to a TGA test result on the same sample being tested in which a precise, specific ratio of molecule(s) of water that constituted water formally associated in the unit cell of a crystal lattice is released (e.g., lost) in the specified test period." (Id.)

BMS relies on the testimony of its expert to explain that "one of ordinary skill would understand this term to mean that the broad peak between approximately 95°C and 130°C corresponds to a weight loss attributable to one water of hydration on thermogravimetric analysis." (Pl. Opening Br. at 28.)

Apotex informs the Court that "[t]hermogravimetric analysis ("TGA") is a technique that measures change in the weight of a sample as a function of temperature. (Desiraju ¶ 66). Such a change might indicate to one of skill in the art that residual solvent, such as water, is lost, perhaps confirming the presence of that solvent." (Defs. Opening Br. at 33.) Apotex argues that the "loss of one water of hydration on thermogravimetric analysis" does not correspond with "the output of the test method", rendering the claim language insolubly ambiguous. (See id.) Moreover, Apotex argues that a "compound of claim 3" cannot lose one water of hydration because the Formula IV structure (which is the compound of claim 3) would be

fundamentally altered if such an event occurred, and it would become a decomposition product. (See id.) Finally, Apotex argues that claim 9 refers to results from both differential scanning calorimetry and thermogravimetric analysis tests, which are mutually exclusive -- performing either test will destroy the tested material, making it impossible to then serially perform the other test. (See id. at 34.)

BMS explained at oral argument that thermogravimetric analysis is destructive testing that will destroy a crystalline monohydrate piece by piece to determine its component parts through physical chemistry testing. (See dkt. entry no. 92, Tr. of Markman Hr'g on Oct. 2, 2012 at 97-100 ("10-2-12 Transcript").)

> MS. BEN-AMI: For each molecule of Dasatinib there's only one water. So if there's 100 percent, you know -- if the experiment is 100 percent perfect in theory, which no experiments are, then you would say all the water was out at that time.
> THE COURT: Okay. But some may be a little bit reluctant --
> MS. BEN-AMI: But you've got the concept correct that water is coming off at one temperature. The rest of it is melting at a different temperature. That's, basically, what it is about.

(Id. at 99-100.) Further, with respect to Apotex's position that the term is confusing because "compound" is not the crystalline monohydrate, BMS contends that experts for both parties understood the meaning of the word in this context and

in light of the patent as a whole. (See Pl. Responsive Br. at 24.) BMS notes particularly that Figure 2 shows both differential scanning calorimetry and thermogravimetric analysis thermograms of the crystalline monohydrate of the compound of formula (IV). (See id.) As the claim's reference, this furthers BMS's argument that a person of ordinary skill in the art would understand the word "compound" to mean the test had been performed on the crystalline monohydrate. (See id.)

Apotex responds with several arguments: (1) without any intrinsic support for such an assumption, BMS presumes that "compound", which does not have a water of hydration to lose, means "crystalline monohydrate", which is accompanied by a water for each chemical structure; and (2) BMS ignores the requirement that the "peak" observed in the differential scanning calorimetry analysis correspond with the loss of the water of hydration. (See Defs. Responsive Br. at 28-29.)

The Court has considered the parties' respective arguments, the patent claims, the specification and the experts' testimonial evidence. The Court agrees with the patentee that one of ordinary skill would understand this term to mean that the broad peak between approximately 95°C and 130°C corresponds to a weight loss attributable to one water of hydration on thermogravimetric analysis. The Court also finds that the term

"compound of claim 3" does not create insoluble ambiguity in light of the graph in Figure 2 of the specification, which shows both differential scanning calorimetry and thermogravimetric analysis thermograms of the crystalline monohydrate of the compound of formula (IV). The Court thus construes the term "which corresponds to the loss of one water of hydration on thermogravimetric analysis" as follows:

"[W]hich corresponds to a weight loss attributable to one water of hydration on thermogravimetric analysis."

9. "[W]hich is further characterized by a weight loss of 3.48% by thermogravimetric analysis between 50° C and 175° C"

The term appears in claim 10 of the '725 Patent. (See '725 Patent, col. 50, lines 6-8.)

BMS proposes that the term be construed to mean "which is further characterized by a weight loss of 3.48% by thermogravimetric analysis between 50° C and 175° C, taking into account variations due to measurement errors and dependent upon the measurement conditions employed." (Joint Statement at 46.)

Apotex states that "[i]n isolation, the phrase would refer to material that is being subjected to the testing. (Id.) If the Court does not find the language "internally contradictory," Apotex asks the Court to recognize that "the language out of

context would indicate that there is an instrumental measured weight loss of the stated amount being sampled between the stated temperature range. However, this claim language is vague and indefinite in the context of the remainder of the claim. The 'weight loss' claim language makes no sense in context, or is not enabled, because a 'compound' does not lose weight." (Id.)

BMS points to support from the specification for its proposed construction: "[t]he TGA shows a 3.48% weight loss from 50 C to 175 C. The weight loss corresponds to a loss of one water of hydration from the compound of Formula (IV)." (Pl. Opening Br. at 29; '725 Patent at col. 45, lines 25-28.)

Apotex complains that the "material that is supposedly supposed to lose the weight is 'the compound of claim 9.' . . . [T]he compound structure of Formula (IV) is not going to lose water unless it is fundamentally changed. Thus, the plain meaning of the claim language seeks to describe an impractical, if not inoperable, circumstance." (Defs. Opening Br. at 34.)

The Court has considered the parties' respective arguments, the patent claim, the specification and the experts' testimonial evidence. The Court agrees with the patentee that one of ordinary skill would understand this term to indicate the material should be destructively tested through differential

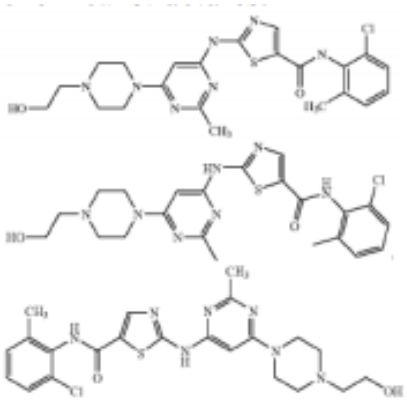
scanning calorimetry or thermogravimetric analysis. The Court also finds that the term "compound of claim 3" does not create insoluble ambiguity in light of the graph in Figure 2 of the specification, which shows both differential scanning calorimetry and thermogravimetric analysis thermograms of the crystalline monohydrate of the compound of formula (IV). The Court thus construes the term "which is further characterized by a weight loss of 3.48% by thermogravimetric analysis between 50° C and 175° C" as follows:

"[W]hich is further characterized by a weight loss of 3.48% by thermogravimetric analysis between 50° C and 175° C, taking into account variations due to measurement errors and dependent upon the measurement conditions employed."

IT IS THEREFORE on this 28th day of March, 2013, **ORDERED** that the Court finds:

(1) the term "a compound or salt thereof selected from the group consisting of" found in claim 6 of United States Patent No. 6,596,746 (the "'746 Patent") is construed as follows: **a compound or its salt ("salt" meaning acidic and/or basic salts formed with inorganic and/or organic acid and bases) selected from the claimed list**, and

(2) the term "'N-(2-Chloro-6-methylphenyl)-2-[[6-[4-(2-hydroxyethyl)-1-piperazinyl]-2-methyl-4-pyrimidinyl]amino-5-thiazolecarboxamide" from the list of chemical names in claim 6 of the '746 Patent is construed as follows: **the compound having the following equivalent chemical structures**



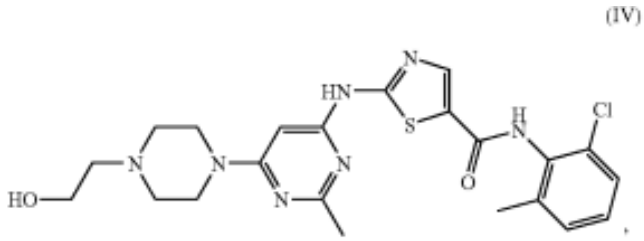
, and

(3) the term "administering to" or "administering orally to", found in claims 7, 44, and 47 of the '746 Patent, as

well as claim 1 of United States Patent No. 7,153,856 ("the '856 Patent") and claims 1, 2, 3, 11, and 27 of United States Patent No. 7,125,875 ("the '875 Patent"), is construed as follows: **to mete out or dispense or to give remedially**, and

(4) the term "a subject in need thereof" found in claims 7, 44, and 47 of the '746 Patent, as well as in claim 1 of the '856 Patent and in claims 1, 2, 3, 11, and 27 of the '875 Patent, is construed as follows: **an animal, including a human, in need thereof**, and

(5) the term "wherein the cancer is resistant to treatment by STI-571", found in claims 9, 10, 12, and 27 of the '875 Patent, is construed as follows: **wherein the cancer [or chronic myelogenous leukemia] exhibits resistance to treatment by STI-571**, and

(6) the term "crystalline monohydrate of the compound of formula (IV) 

", found in claims 1, 3, and 12 of United States Patent No. 7,491,725 ("the '725 Patent"), is hereby construed as follows: **the monohydrate of the compound of formula (IV) in a crystalline form**, and

(7) the term "which is characterized by an x-ray powder diffraction pattern substantially in accordance with that shown in FIG. 1", found in claim 1 of the '725 Patent, is construed as follows: **which is characterized by an x-ray powder diffraction pattern that is substantially identical to those shown in FIG. 1 taking into account variations due to measurement errors and dependent upon the measurement conditions employed, but not taking into account the exact order of intensity of the peaks**, and

(8) the term "the compound of claim 1" or "the compound of claim 3" or "the compound of claim 9" or "the compound of claim 12", found in claims 2, 4, 5, 8-11, and 13-16 of the '725 Patent, is construed as follows: **the monohydrate of the compound of formula (IV) in a crystalline form**, and

(9) the term "a process for preparing the compound of claim 3", found in claims 6 and 7 of the '725 Patent, is construed as follows: **a process for preparing the crystalline monohydrate of the compound of formula (IV)**, and

(10) the terms "[w]hich is characterized by differential scanning calorimetry thermogram and a thermogravimetric analysis substantially in accordance with that shown in FIG. 2", "[being further] characterized by a differential scanning calorimetry having a broad peak between

approximately 95° C and 130° C", and "wherein the differential scanning calorimetry further has a peak at approximately 287° C", found in claims 1, 9, 11, and 12 of the '725 Patent, are construed as follows: **Which is characterized by differential scanning calorimetry thermogram and thermogravimetric analysis patterns that are substantially identical to those shown in FIG. 2, having one peak at approximately 287° C and one broad peak between approximately 95° c and approximately 130° C; being further characterized by a differential scanning calorimetry having a broad peak between about 95° C and about 130° C; characterized by differential scanning calorimetry with a peak located at about 287° C which corresponds to the melt of the dehydrated form of the compound of formula (IV)**, and

(11) the term "which is characterized by an x-ray powder diffraction pattern (CuK_α λ=1.5418 Å at a temperature of about 23°C.) comprising four or more 2θ values selected from the group consisting of 18.0±0.2, 18.4±0.2, 19.2±0.2, 19.6±0.2, 21.2±0.2, 24.5±0.2, 25.9±0.2, and 28.0±0.2", found in claim 3 of the '725 Patent, is construed as follows: **which is characterized by an x-ray powder diffraction pattern taken with CuK_α λ=1.5418 Å at a temperature of about 23°C, having at least four 2θ values selected from the group consisting of 18.0±0.2, 18.4±0.2,**

19.2±0.2, 19.6±0.2, 21.2±0.2, 24.5±0.2, 25.9±0.2, and 28.0±0.2, and

(12) the term "characterized by unit cell parameters approximately equal to the following dimensions:

Cell dimensions: a(Å)=13.8632(7); b(Å)=9.3307(3); c(Å)=38.390(2);

Volume=4965.9(4) $Å^3$

Space group Pbca

Molecules/unit cell 8

Density (calculated) (g/cm^3) 1.354", found in claim 5 of the '725 Patent, is construed as follows: **characterized by unit cell parameters approximately equal to the following dimensions:**

Cell dimensions: a(Å)=13.8632(7); b(Å)=9.3307(3); c(Å)=38.390(2);

Volume=4965.9(4) $Å^3$

Space group Pbca

Molecules/unit cell 8

Density (calculated) (g/cm^3) 1.354, and

(13) the term "wherein the compound is substantially pure", found in claims 8, 15, and 16 of the '725 Patent, is construed to mean: **the compound itself having a purity greater than 90 percent**, and

(14) the term "which corresponds to the loss of one water of hydration on thermogravimetric analysis", found in claims 9 and 12 of the '725 Patent, is construed as follows: **which corresponds to a weight loss attributable to one water of hydration on thermogravimetric analysis**, and

(15) the term "which is further characterized by a weight loss of 3.48% by thermogravimetric analysis between 50° C and 175° C", found in claim 10 of the '725 Patent, is construed as follows: **which is further characterized by a weight loss of 3.48% by thermogravimetric analysis between 50° C and 175° C, taking into account variations due to measurement errors and dependent upon the measurement conditions employed**.

s/ Mary L. Cooper
MARY L. COOPER
United States District Judge